I. The Amendments

Applicants have canceled claims 4, 5, 8-17, 32, 34 and 35 to promote prosecution efficiency, to more particularly define the invention and to obtain early allowance of patentable subject matter. However, Applicants do not acquiesce to any of the grounds for rejection of any of the now canceled claims that are supported by the specification, particularly on pages 8-15. Applicants, thus, reserves the right to pursue the subject matter in a later continuing application. Therefore, as a result of the cancellation, claims 1-3, 6, 7, 18-31, and 33 are presently pending. Support for adding amending claim 18 can be found in the specification at page 13, lines 22-23. Support for adding amending claim 27 can be found in the specification at page 13, lines 15-19.

Applicants assert that no new matter has been introduced as a result of the amendments.

II. Formal Matters

Applicants acknowledge that the present application was filed under 35 USC 371 and, as such, was not subjected to restriction.

III. Sequence Listing

Applicants filed a response to the Notice to Comply in a separate mailing dated May 22, 2000.

IV. Rejection under 35 U.S.C. §112, Second Paragraph

Claims 4, 5, 8-17, and 27-34 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject which applicant regards as the invention.

The rejections to claims 4, 5, 8-17, 32 and 34 have been made moot by the present claim cancellations. For the remaining indefiniteness rejections to the remaining rejected claims, Applicants assert that the claims are definite.

The Examiner indicated that claim 28 lacks sufficient number of elements to support the

preamble recitation for a composition. Applicants direct the Examiner's attention to the last phrase in the claims reciting "and a pharmaceutically acceptable excipient". Thus, the claim contains the requisite elements to be a composition.

The Applicants also direct the Examiner to claim 33 which is not a kit but rather a method; therefore, the indefiniteness rejection to a kit with claim 32 is not applicable.

Claim 27 was rejected as being indefinite for reciting the phrase "condition characterized by OB resistance". While Applicants consider this phrase to be definite and be supported by written description on specification page 13, lines 15-23, Applicants have amended the phrase to recite the biological basis of OB resistance that results in the necessity of increasing or inducing OB receptor expression, the result of which is achieved in the present invention with the claimed OB receptor inducers. Thus, claim 27 is definite in characterization of the patient population for which treatment is applicable.

In view of the above comments, along with the amendments to the pending claims, Applicants believe that the rejections for indefiniteness have been overcome. Applicants respectfully request that the rejections on this ground for pending claims 27-31 and 33 be withdrawn.

V. Rejection under 35 U.S.C. §112, First Paragraph

Claims 15-18, 20-24, 27-31 and 34-35 are rejected under 35 U.S.C. §112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Applicants respectfully traverse this rejection.

The rejections to claims 15-17, 34 and 35 have been made moot by the present claim cancellations. Applicants however maintain that the cancelled claims are enabled as supported in the specification as previously stated and Applicants reserve the right to pursue the cancelled subject matter in a continuing application. For the remaining enablement rejections to the remaining rejected claims, Applicants assert that the claims are enabled.

The Examiner rejected claims 18 and 20-24 on the basis that the specification does not enable treatment of obesity with any OB receptor expression inducer. The Examiner further contends that expression regulation is unpredictable. Applicants contend conversely that compounds including cytokines are well known to one of ordinary skill in the art and that such a person would consider the invention reasonably to include any molecule that is known or could readily be evaluated with the methods of the invention as described on specification beginning on page 16 continuing to page 19. The determination of a compound having the requisite activity is not undue. According to the courts, Applicants need not prepare and test each and every possible combination of compounds that could induce OB receptor expression encompassed by the claims. The relevant inquiry in determining whether a particular claim is supported by the specification is whether the specification contains sufficient teachings **regarding the subject matter of the claim** as to enable one skilled in the art to make and use the invention. *In re Moore*, 169 USPQ 236, 239 (C.C.P.A. 1971; emphasis added). Thus, if one were interested in performing an assay, for example, it would be within the purview of a skilled worker to consult the relevant art -- e.g., solid-phase assays -- to ascertain appropriate inducers for use as disclosed herein. Arguably, even if some experimentation is necessary, enablement is not precluded. *Atlas Powder Co. v. E. I. duPont de Nemours & Co.*, 224 USPQ 409, 413 (Fed. Cir. 1984).

Thus, Applicants argue that the claims 18 and 20-24 are enabled and supported by the teachings in the specification. However, to expedite prosecution and allowance of the claims, Applicants have amended claim 18 to recite cytokine inducers as similarly recited in claims 28-31. The Examiner has rejected the latter claims on the same grounds in that the use of any cytokine in inducing expression of the OB receptor is equally unpredictable. The specification provides sufficient enablement for a number of cytokines that exhibit OB receptor-inducing activity. As such, Applicants contend that the claims as presently pending are enabled.

The Examiner also rejects claims 27 for lack of enablement as to the scope of conditions characterized by OB resistance. Applicants incorporate the arguments made in the indefiniteness section herein for providing support in the specification regarding enablement of the claim as

originally drafted. Thus, Applicants assert that the claim is enabled as originally written and as presently amended.

In view of the foregoing arguments or amendments, Applicants contend that the rejections have been overcome and respectfully request that the rejections be withdrawn directed to the pending claims 18, 20-24 and 27-31.

VI. Art-based Rejections under 35 U.S.C. §102(b) and or §103(a)

A. Claims 8-14 and 15-17 are rejected under 35 U.S.C. §102(b) as being anticipated by, or in the alternative, under §103(a) as being obvious over Friedman et al. ('309), Grunfeld et al., Pelleymounter et al. or Halaas et al.

The rejections to claims 8-14 and 15-17 have been made moot by the present claim cancellations. Applicants however maintain that the cancelled claims are patentable over the cited art and Applicants reserve the right to pursue the cancelled subject matter in a continuing application.

B. Claims 33-35 are rejected under 35 U.S.C. §102(b) as being anticipated by, or in the alternative, under §103(a) as being obvious over Friedman et al. ('309).

The rejections to claims 34 and 35 have been made moot by the present claim cancellations. Applicants however maintain that the cancelled claims are patentable over the cited art and Applicants reserve the right to pursue the cancelled subject matter in a continuing application.

For claim 33, the Examiner contends that Friedman et al. discloses antibodies to the OB protein and teach that the antibodies can be used in diagnostic methods as the basis for detection of disorders associated with the OB protein. Friedman et al. neither discloses nor suggests the use of an OB antibody for use in assaying a disease marker for an inflammatory response. Friedman et al. merely discloses the making and use of an OB antibody for screening patients where abnormal weight is a factor (see specification page 70, lines 1-3). Therefore, Applicants

argue that the rejection for anticipation as well as obviousness be withdrawn in view of the absence of any teachings or suggestions in Friedman et al. encompassing the present invention as recited in claim 33.

C. Claims 28-31 are rejected under 35 U.S.C. §102(b) as being anticipated by, or in the alternative, under §103(a) as being obvious over Grunfeld et al.

The Examiner contends that Grunfeld et al. teach that "endotoxin and cytokines induce the expression of leptin/OB in response to infection" and therefore "anticipate or render obvious the claims for a composition of the OB protein and a cytokine" despite use intentions. Applicants direct the Examiner to the teachings in Grunfeld et al. where the correlation of treatment with either endotoxin or a cytokine resulted in an increase in leptin expression. **Nowhere** in the publication does Grunfeld teach or remotely suggest that a OB protein would be useful in combination with endotoxin or a cytokine as claimed in the present invention. Applicants direct the Examiner to specification pages 22, line 9 continuing to page 24, line 6 where mice treated with both OB protein and LPS lost weight. The Grunfeld et al. publication does not disclose or suggest the use of both inducer and OB protein to facilitate weight loss.

Therefore, Applicants argue that the rejection for anticipation as well as obviousness be withdrawn in view of the absence of any teachings or suggestions by Grunfeld et al. in encompassing the present invention as recited in claims 28-31.

D. Claims 1-7, 18-26, 27, 28-31 are rejected under §103(a) as being obvious over Grunfeld et al. Applicants respectfully traverse this rejection.

The Examiner contends that since Grunfeld et al. teaches the induction of OB protein in response to infection mediated by LPS and cytokines, it would have been obvious to use the OB protein alone or in conjunction with the inducers to regulate energy metabolism during an inflammatory response associated with the OB protein.

Applicants point out that the cited art does not suggest the use of OB protein as the

therapeutic agent with or without an OB receptor inducer to mediate energy metabolism in an inflammatory response. Grunfeld et al., as summarized above, report that OB protein increases as a result of endotoxin or cytokine exposure; the reference does not teach or suggest that the OB protein that results from endotoxin exposure could be separately used or used in combination with endotoxin or cytokines to ameliorate an inflammatory response resulting in survival thereby overcoming a deleterious response that is caused by exposure to inflammatory agents such as endotoxin.

Therefore, Applicants argue that the rejection for obviousness be withdrawn in view of the absence of any teachings or suggestions by Grunfeld et al. in encompassing the present invention as recited in claims 1-7, 18-26, 27, 28-31.

VII. Summary

Applicants believe that a complete response is provided in the foregoing amendments and remarks to each issue and grounds for rejection and objection raised by the Examiner. Applicants submits that patentable subject matter exists with regard to the pending claims and therefore respectfully requests favorable action and entry of the presents Amendments and Response. The application is now believed to be in proper condition for allowance and early notification of allowance is earnestly solicited. The Examiner is invited to telephone the undersigned if it would be deemed helpful to advance the application.

10/20/00
Date

Emily Holmes, Reg. No. 40,652

THE SCRIPPS RESEARCH INSTITUTE
10550 North Torrey Pines Road
Mail Drop TPC-8
La Jolla, California 92037
858-784-2937
ch:c:\wp\oa\scr1832p.rep